

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent application of: MICHAEL J. WELSH and JOHN A. WEMMIE

For: NOVEL COMPOSITIONS AND METHODS FOR MODULATION OF THE ACID-SENSING ION CHANNEL (ASIC) FOR THE TREATMENT OF ANXIETY AND DRUG ADDICTION,

the specification of which is being transmitted herewith.

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

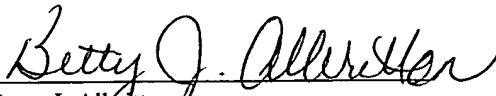
Attached are Forms PTO/SB/08A and 08B (formerly Form PTO-1449) listing the relevant art known to the applicant herein. The Examiner is requested to consider the references and make them of record. This application also relies, under 35 U.S.C. § 120, on the earlier filing date of prior application Serial No. 10/112,290, filed on March 29, 2002. Each of the references listed on the earlier filed Forms PTO/SB08A and 08B were submitted to the Patent Office in the prior application and, therefore, are not required.

Applicants submit herewith patents, publications or other information, of which they are aware that they believe may be material to the examination of this application, and in respect of which, there may be a duty to disclose. Legible copies of all items listed in Forms PTO/SB/08A

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Betty J. Albritton  
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and 08B (formerly Form PTO-1449) accompany this information statement, except those identified above.

The filing of this information disclosure statement shall not be construed as a representation that a search has been made (37 C.F.R. § 1.97(g)), an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

The filing of this information disclosure statement shall not be construed as an admission against interest in any manner. (Notice of January 9, 1992, 1135 O.G. 13-25, at 25.)

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Lila Akrad", with a large, stylized initial "L" and a cursive "A".

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-bj- -

Attorneys of Record

Substitute for form 1449A/PTO			<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>			Application Number	10/112,280
			Filing Date	March 29, 2002
			First Named Inventor	Welsh, Michael J.
			Art Unit	1614
			Examiner Name	
(Use as many sheets as necessary)			Attorney Docket Number	P05405US0
Sheet	1	of	?	

U.S. PATENT DOCUMENTS					
Examiner Initials *	Cite No. <sup>1</sup>	Document Number Number - Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	US- 6,100,269	08/08/00	Merouane, Bencharif	
	2	US- 6,218,383	04/17/01	Merouane, Bencharif	
	3	US- 6,284,731	09/04/01	Maccicchini, Maria-Luisa	
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Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>

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<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.

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Substitute for form 1449B/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Application Number</b>	
		<b>Filing Date</b>	September 10, 2003
		<b>First Named Inventor</b>	WELSH, Michael J., et al.
		<b>Group Art Unit</b>	1614
		<b>Examiner Name</b>	
<b>Sheet</b>	1	of	3
		<b>Attorney Docket Number</b>	P05405US01

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1	BENSON, "Acid Evoked Currents in Cardiac Sensory Neurons A Possible Mediator of Myocardial Ischemic Sensation," Oregon Health Sciences University, pp. 921-928 (1999)	
	2	CHEN, "A sensory Neuron-Specific, Proton-Gated Ion Channel," Proc. Natl. Acad. Sci., Vol. 95, pp. 10240-10245, (August 1998).	
	3	HRUSKA-HAGEMAN, "Interaction of the Synaptic protein PICK1 (Protein Interacting with C Kinase 1) with the non-voltage gated sodium channels BNC1 (brain Na <sup>+</sup> -channel 1) and ASIC (Acid-Sensing Ion Channel)," Biochem J., Vol. 361, No. Pt 3, pp. 443-50 (February 1, 2002).	
	4	WELSH, "ASIC and BNC1 Mediate Proton-Gated Currents in Hippocampal Neurons," Society for Neuroscience Abstracts, Vol. 27 No. 2 pp. 2416 (2001)	
	5	WELSH, "Drasic, ASIC and BNC1 form Heteromultimeric Proton-Gated Channels in Mouse DRG Neurons," Society for Neuroscience Abstracts, Vol. 27, No. 2, pp. 2414 (2001).	
	6	WELSH, "The Acid-Activated Ion Channel ASIC Contributes to Synaptic Plasticity, Learning and Memory" Neuron, Vol. 34, 463-477, April 25, 2002	
	7	WEMMIE, "The Role of ASIC, An Acid Sensing Ion Channel in Synaptic Plasticity, Learning, and Memory," Society for Neuroscience Abstracts, Vol. 27 No. 2, pp. 2416 (2001).	
	8	XIE, "The Drastic Channel Subunit Functions in Detection of Touch and Acid," Society for Neuroscience Abstracts, Vol. 27, No. 2, pp. 2168 (2001)	
	9	XIE, "Drastic Contributes to pH-Gated Currents in Cultured DRG Sensory Neurons by Forming Multimeric Cation Channels, Society for Neuroscience Abstracts, Vol. 27, No. 2, pp. 2169 (2001)	
	10	BENSON, "Heteromultimers of DEG/ENaC Subunits form H <sup>+</sup> -gated channels in mouse sensory neurons" PNAS, vol. 99, no. 4, pp 238-2343 (February 19, 2002)	
	11	LINGUEGLIA "A Modulatory Subunit of Acid Sensing Ion Channels in Brain and Dorsal Root Ganglion Cells", The Journal of Biological Chemistry, Vol. 272, No. 47, pp. 29778-29783 (November 21, 1997)	
	12	ESCOUBAS "Isolation of a Tarantula Toxin Specific for a Class of Proton-gated Na <sup>+</sup> Channels" The Journal of Biological Chemistry, Vol. 275, No. 33, pp. 25116-25121, August 18, 2000	
	13	ALLEN "Modulation of ASIC Channels in Rat Cerebellar Purkinje Neurons by Ischaemia-related Signals" Journal of Physiology (2002) 543,2m oo, 521-529	

Examiner Signature		Date Considered	
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Approved for use through 10/31/2002. OMB 0651-0031

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Substitute for form 1449B/PTO		<b>Complete if Known</b>	
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		Filing Date	September 10, 2003
		First Named Inventor	WELSH, Michael J., et al.
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Sheet 2 of 3	Attorney Docket Number	P05405US01	

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	14	ALVAREZ de la Rosa, "Distribution, Subcellular Localization and Ontogeny of ASIC1 in the Mammalian Central Nervous System, Journal of Physiology (2003) 546.1, pp. 77-87	
	15	DRISCOL, "Protons at the Gate: DEG/ENaC Ion Channels Help Us Feel and Remember" Neuron, Vol. 34, 336-340, April 26, 2002	
	16	EVERITT "Emotion and Motivation: The Role of the Amygdala, Ventral Striatum, and Prefrontal Cortex" Neuroscience and Biobehavioral Reviews 26 (February 20, 2002) 321-352	
	17	FANSELOW, "Why We Think Plasticity Underlying Pavlovian Fear Conditioning Occurs in the Basolateral Amygdala" Neuron, Vol. 23, 229-232, June, 1999.	
	18	GARCIA-ANOVEROS "BNaC1 and BNaC2 Constitute a New Family of Human Neuronal Sodium Channels Related to Degenerins and Epithelial Sodium Channels" Pro. Natl. Acad. Sci. USA, Vol. 94, pp. 1459-1464, February 1997	
	19	HYMAN "Addiction and the Brain: The Neurobiology of Compulsion and its Persistence" Nature Reviews/Neuroscience, Macmillan Magazines, Ltd., Vol. 2, October 2001	
	20	MCKERNAN "Fear Conditioning Induces A Lasting Potentiation of Synaptic currents <i>in vitro</i> " Nature, Vol 390, December 1997	
	21	PRICE "The Mammalian Sodium Channel BNC1 is Required for Normal Touch Sensation" Nature, Vol. 407, October 26, 2000	
	22	PRICE "The DRASIC Cation Channel Contributes to the Detection of Cutaneous Touch and Acid Stimuli in Mice" Neuron, Vol. 32, 1071-1083, December 20, 2001	
	23	ROGAN "Fear Conditioning Induces Associative Long-Term Potentiation in the Amygdala" Nature, Vol 390, December 1997	
	24	SHEPHERD "Olfactory Bulb In: The Synaptic Organization of the Brain" Ed. 4 No. 5, pp. 159-203, 1998 New York and Oxford	
	25	MAGAZANIK "Characterization of Acid-Sensitive Ion Channels in Freshly Isolated Rat Brain Neurons" Neuroscience Vol. 110, No. 4, pp. 723-730, 2002	
	26	FOX "Anatomical Pathways and Molecular Mechanisms for Plasticity in the Barrel Cortex" Neuroscience Vol. 111, No. 4, pp. 799-814, 2002	

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		Filing Date	September 10, 2003
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	27	GRUOL "Hydrogen Ions Have Multiple Effects on the Excitability of Cultured Mammalian Neurons" Brain Research 183 (1980) 247-252	
	28	IMMKE "Lactate Enhances the Acid-Sensing Na <sup>+</sup> Channel on Ischemia-sensing Neurons" Nature Neuroscience, Vol. 4, No. 9, September 2001	
	29	KRISHTAL "A 'Receptor' For Protons in Small Neurons of Trigeminal Ganglia: Possible Role in Nociception" Neuroscience Letters, 24 (1981) 243-246	
	30	KRISHTAL "Rapid Extracellular pH Transients Related to Synaptic Transmission in Rat Hippocampal Slices" Brain Research, 436 (1987) 352-356	
	31	LOWRY "A Flexible System of Enzymatic Analysis" Academic Press 1972 New York and London	
	32	OLSON "An Acid Sensing Ion Channel (ASIC) Localizes a Small Primary Afferent Neurons in Rats" Rapid Science Ltd., Vol. 9, No. 6, April 1998	
	33	WELSH "Biochemical Basis of Touch Perception: Mechanosensory Function of Degenerin/Epithelial Na <sup>+</sup> Channels" The Journal of Biological Chemistry, Vol. 277, No. 4, January 25, 2002 pp 2369-2372	
	34	WALDMANN "A Proton-gated Cation Channel Involved in Acid-sensing" Nature, Vol. 386, March 13, 1997	

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